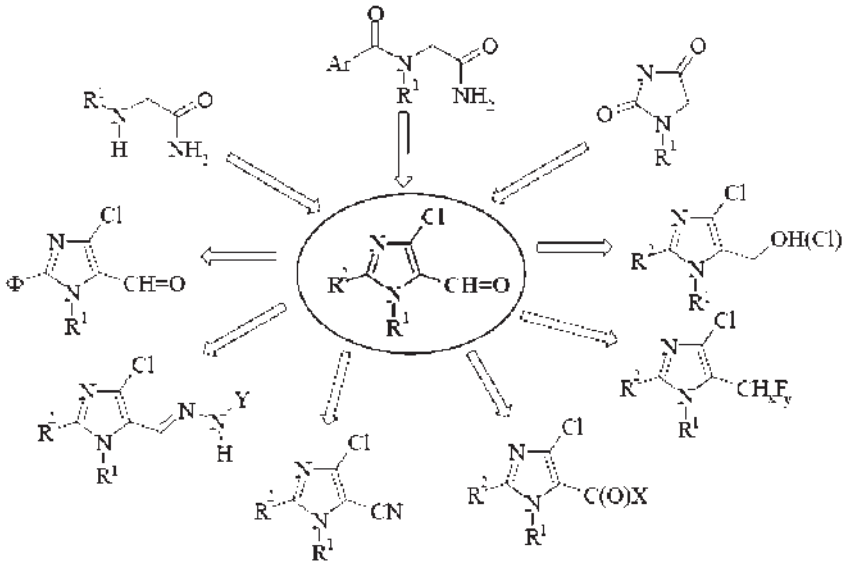
A targeted functionalization of the imidazole cycle with some pharmacophore fragments has been performed in the 2nd, 4th and 5th positions on the basis of a wide range of imidazole derivatives containing some groups facilitating further structural modification. Bioscreening of a considerable number of synthesized substances showed that this type of imidazoles are effective systems for further more detailed investigation of the leading compounds to develop highly effective drugs.



R^1 = Alk, Ar; R^2 = H, Cl, Br, Ar, OAlk, SAlk, NAlk, N_3, NH_2; Φ = OAlk, SAlk, NAlk, N_3, NH_2

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THE INFLUENCE OF MELATONIN ON GLUTATHIONE-S-TRANSFERASE ACTIVITY IN THE KIDNEYS OF RATS UNDER ALLOXAN-INDUCED DIABETES

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Diabetes mellitus is the most common endocrine disease. Experimental model of alloxan diabetes is an example of free radical pathology and is accompanied by_impairment of oxidant-antioxidant balance in animals. Melatonin is one of the most powerful endogenous antioxidants, along with the fact that it stimulates glucose utilization in tissues, increases the concentrations of ATP and creatine phosphate, stimulates deposites of glycogen in the tissues.

The aim of the research was to assess changes of glutathione-S-transferase activity in the kidneys of rats under the experimental alloxan-induced diabetes and administration of melatonin.

Experiments were performed (coducted) on 50 mature white male rats with body weight 160-180 g. Alloxan-induced diabetes was induced by intraperitoneal injection of 5% solution of alloxan monohydrate in the dose of 150 mg/kg. Animals were divided into groups: 1) control animals; 2) animals with manifested diabetes (basal glycemia 12,8-17,2 mmol /l); 3) animals with manifested diabetes which underwent intragastric administration of melatonin daily in the dose of 10 mg/kg at 8.00 a.m. The animals were decapitated under light ether anesthesia on the 7th and the 14th day of the drug administration. In post-nuclear supernatants of homogenates of renal cortical layer activity of glutathione-S-transferase was measured. The results were processed statistically using nonparametric methods of variation statistics using STATISTICA 7.

It has been found out, that an experimental model of alloxan-induced diabetes was accompanied by increased activity of glutathione-S-transferase in cortical layer of the rats' kidneys by 43% and 95% above the control on the 7th and the 14th days of the experiment respectively. The increase of glutathione-S-transferase activity in the kidneys of diabetic rats probably is related to increased disposal of secondary products of lipid peroxidation and other oxidized substances due to conjugation with glutathione.

Administration of melatonin to animals with alloxan-induced diabetes caused decease of glutathione-S-transferase activity in the kidney in comparison with untreated animals, but it remained higher than the level of control animals on the 7th day on 30%, on the 14th day on 37%.

Antioxidant properties of melatonin are likely related to both direct disposal of reactive oxygen species and the influence of melatonin on the expression of genes that are responsible for synthesis of antioxidant enzymes.